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EXAMINER

KERR, KATHLEEN M

ART UNIT

PAPER NUMBER

1652

DATE MAILED: 07/02/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/509,608

Applicant(s)

WEBER ET AL.

Examiner

Kathleen M Kerr

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 February 0422.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 27-53 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 27-53 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: |

DETAILED ACTION

Application Status

1. In response to the previous Office action, a first Office action on the merits (Paper No. 10 mailed January 14, 2002), Applicants filed an amendment and response. Applicant's amendment cancelled all previously pending Claims 1-26 and added new claims 27-53. Claims 27-53 are pending in the instant application and will be examined herein.

Priority

2. As previously noted, the instant application is granted the benefit of priority for International Application No. PCT/EP98/06134 filed on September 28, 1998. The instant application is also granted the benefit of German application 197 44 212.9 filed on September 30, 1997 in the absence of a translation since no intervening art has been identified.

Drawings

3. The drawings filed on April 22, 2002 have been approved by the Draftsmen and are, therefore, entered as formal drawings acceptable for publication upon the identification of allowable subject matter.

Withdrawn - Objections to the Specification

4. Previous objection to the specification for containing German words is withdrawn by virtue of Applicants' amendment.

Maintained - Objections to the Specification

5. Previous objection to the specification for lacking an Abstract is maintained. Applicants supplied an Abstract in the amendment; however, this Abstract must be on a separate sheet of paper as previously noted. Moreover, the completeness of the Abstract in the amendment is wholly inadequate. It is noted that in many databases and in foreign countries, the Abstract is crucial in defining the disclosed subject matter, thus, its completeness is essential. The Examiner suggests the inclusion of the enzyme names, in full and their abbreviations, for completeness.

Status of Pending Claim Objections/Rejections

6. All previously pending objections/rejections are herein withdrawn by virtue of Applicant's cancellation of all previously pending claims. Wherein a new rejection is made herein and the issue had been previously raised, the Examiner will address Applicants comments in the new rejections below.

NEW OBJECTIONS/REJECTIONS

Claim Objections

7. Claim 36 is objected to under 37 C.F.R. § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the

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claim(s) in independent form. Claim 36 does not incorporate all the limitations of Claim 27 into the dependent claim. The scope of Claim 36 is wholly different from that of Claim 27.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 27-29, 32-35, and 51-53 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The instant claims are all drawn to methods of producing intermediate products in the biosynthesis of ergosterol. The term "intermediate products" is unclear as to its metes and bounds as noted in the previously pending claims. Applicants argue that this term is definite based on "non-limiting" examples in the specification. The Examiner disagrees. It is unclear where the metes and bounds of ergosterol biosynthesis lie. Biosynthesis and metabolism in organisms are complex, intertwined processes. Without clear definition of what compounds are encompassed by the term "intermediate products", one could argue that glucose was an intermediate product since it is involved in most biosynthetic processes. The metes and bounds of the claims must be clearly defined so that one of skill in the art understands exactly where the patent coverage begins and ends. Appropriate correction is required.

9. Claims 27-53 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The terms "t-HMG gene" and "SAT1" are wholly unclear. On page

20, the specification describes tHMG by reference to Basson *et al.* 1986; however, the HMG-CoA reductase gene taught in Basson *et al.* is called HMG1. On page 23, the specification describes SAT1 by reference to Yang *et al.* 1996; however, the acyl transferase gene taught in Yang *et al.* is called ARE1. It is unclear if some t-HMG gene exists or is it Applicants' term for any HMG-CoA reductase gene. The definition of SAT1 is wholly unclear.

10. Claims 27-35 and 52 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In Claim 27, the final step produces ergosterol while the method is drawn to a method of making ergosterol or one or more intermediate products of its biosynthesis. Thus, how the method steps produce intermediates is unclear since, as written, the method steps only produce ergosterol. Appropriate correction is required.

11. Claims 37-42 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 37-39 are drawn to exact plasmids YepH2, YDpUHK3, and pADL-SAT1, respectively. However, the composition of the plasmids noted in the claims is drawn to *any* ADH promoter, *any* t-HMG gene, *any* TRP-terminator, *any* kanamycin resistance gene, *any* ura3 gene, and *any* SAT1 gene as evidenced by the article "a" preceding each component of the plasmids. Plasmids YepH2, YDpUHK3, and pADL-SAT1 are particular and exact plasmids whose production is described in the specification using *S. cerevisiae* DNA (see pages 20-23). These plasmids do not contain any t-HMG or SAT1 gene but contain the *S. cerevisiae* t-HMG and SAT1 genes. Thus, the variability indicated in the claims is confusing.

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12. Claim 42 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase “a sterol with a 5,7-diene structure” is unclear since only one 5,7-diene structure is available in the Markush group of Claim 41, that is ergosta-5,7-dienol. The article “a” indicates more than one product is produced. Appropriate clarification is required.

13. Claims 43, 44, and 46-51 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In Claims 43 and 44, the term “flanked” is unclear. Does the t-HMG gene require an ADH-promoter and a TRP-terminator on each side (where each component flanks)? Or can the ADH-promoter be on one side while the TRP-terminator be on the other (together the components flank)? If this second option, must the promoter be 5’ and the terminator be 3’? Appropriate clarification is required.

14. Claim 53 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 53 is incomplete because it omits essential steps, such omission amounting to a gap between the steps. See M.P.E.P. § 2172.01. The claim is drawn to methods of producing ergosterol while the steps only include gene expression. Such steps do not inherently produce ergosterol. Appropriate correction is required.

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The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

15. Claims 27-31, 33-36, and 43-53 are rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The instant claims are drawn to yeast strains and expression cassettes containing genes defined only by the enzyme they encode, wherein the enzyme is defined only by name, which name is indicative of a function. The instant claims are also drawn to methods of making ergosterol using genes that are defined only by function.

The Court of Appeals for the Federal Circuit has recently held that a “written description of an invention involving a chemical genus, like a description of a chemical species, ‘requires a precise definition, such as be structure, formula [or] chemical name,’ of the claimed subject matter sufficient to distinguish it from other materials.” *University of California v. Eli Lilly and Co.*, 1997 U.S. App. LEXIS 18221, at *23, quoting *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical

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characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these.

The instant specification describes the genes to be used in the claimed methods by virtue of function alone. No structures, other than specific species of genes, are described. No relation between the structure of the species and function is described. Thus, one of skill in the art would be required to predict new genes for use in the claimed methods based solely on their function, or the function of their encoded proteins. Such methods would not be predictably considering the minimal structural information provided in the specification.

The instant rejection was previously set forth; Applicants presented no arguments in their cancellation of the claims.

16. Claims 32 and 37-42 are rejected under 35 U.S.C. § 112, first paragraph, enabling deposit, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. To practice the instant methods or to make the claimed products, one of skill in the art is required to use YEpH2, YDpUHK3, and pADL-SAT1 plasmids or AH22 cells. The instant specification contains no deposit information concerning these plasmids and/or cells. To enable the instant claims by enabling the deposit of YepH2, YDpUHK3, and pADL-SAT1 plasmids, the following items are required: (1) the accession number assigned by the depository, (2) the date of deposit, (3) a brief description of the deposit, (4) the name and full address of the depository (37 C.F.R. § 1.801 - 1.809) (those which are in bold have not been fulfilled by the instant specification), and (5) the record must also contain a statement certifying that all restrictions on accessibility to said deposit be irrevocably removed

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by Applicant upon the granting of the patent (see M.P.E.P. § 2404.01); this statement may be certified by Applicants or Applicants' representative. An alternative to the deposit of the exact plasmids is the deposit of all precursor plasmids required to produce the claimed plasmids as described in the specification.

Applicants argue in response to the previous rejection that YEpH2, YDpUHK3, and pADL-SAT1 plasmids and AH22 cells need not be deposited. The Examiner agrees that AH22 cells need not be deposited by virtue of their ubiquitous nature in the art. However, notice is herein made to Applicants that if a patent is granted on claims involving AH22 cells and at any time during the patent term AH22 cells are no longer publicly available for any reason, said patent could be invalidated in its entirety. The lack of a deposit of AH22 cells as related to the instant application risks the public availability of AH22 cells and the validity of any patent. The Examiner disagrees that the plasmids need not be deposited because instructions of how to make said plasmids are enclosed in the specification. The starting materials, Yep13 (Fishhoff *et al.* 1984), YdpU (Berben *et al.* 1991), and pGEM-T (Mezei and Storts 1994) would have to be publicly available for this argument to be persuasive. Thus, the claimed plasmids or all starting materials, as described in the application, must be publicly available to enable the claimed plasmids.

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

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A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

17. Claim 53 is rejected under 35 U.S.C. § 102(b) as being anticipated by Saunders *et al.* (EP 0 486 290 A2 – IDS reference). The instant claims are drawn to methods of making an ergosterol intermediate product by expressing a gene for HMG-CoA reductase in a microorganism from a plasmid.

Saunders *et al.* teach methods of making squalene, an ergosterol intermediate product, using *S. cerevisiae* transformed with a gene encoding HMG-CoA reductase activity (see Abstract).

Conclusion

18. Claims 27-53 are not allowed for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R.

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§ 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (703) 305-1229. The examiner can normally be reached on Monday through Friday, from 8:30am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



PONNATHAPUACHUTAMURTHY
SUPERVISORY PATENT EXAMINER
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KMK
July 1, 2002